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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,619	08/10/2001	Wilson Burgess	061525-5005	2963

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EXAMINER	
CHORBAJI, MONZER R	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,619	BURGESS ET AL.	
	Examiner	Art Unit	
	MONZER R. CHORBAJI	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This non-final action is in response the amendment received on 08/15/2005

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

2. Claim 82 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 82, lines 1-2, applicant recites the feature "a combination of hard and soft tissue". The meaning of this term is not understood in terms of the type of a tissue that have both soft and hard tissue combinations. Explanation and/or rephrasing is needed to understand the meaning of claim 82.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

4. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

5. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim 77 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of copending Application No. 10/133,631 in view of Hanna et al (Free Rad. Res. Comms-IDS).

This is a provisional obviousness-type double patenting rejection.

Claims 1 and 3 of Application No. 10/133,631 teach a method for sterilizing tissues where a stabilizer is added and followed by an irradiation step. However, claims 1 and 3 fail to teach using dipeptide as stabilizers and gamma irradiation. The Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with a gamma irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time was made to modify the method claims of the copending Application No. 10/133,631 by including the dipeptide carnosine as taught by the Hanna reference since carnosine is known to protect irradiated biological material (page 265, lines 1-4).

7. Claim 77 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-4, 37 and 41 of US Application No. 10/024,043.

Claims 2-4, 37 and 41 of US Application No. 10/024,043 fully suggest claim 77 of Application No. 09/925,619.

8. Claim 77 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-4, 37 and 41 of US Application No. 10/379,789.

Claims 2-4, 37 and 41 of US Application No. 10/379,789 fully suggest claim 77 of Application No. 09/925,619.

9. Claims 86 and 97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 98-99 and 104 of copending Application No. 09/942,941 in view of Hanna et al (Free Rad. Res. Comms-IDS).

Claims 98-99 and 104 of Application No. 09/942,941 teaches a method for sterilizing monoclonal immunoglobulin, which is a protein, where a stabilizer is added and followed by an irradiation step. However, claims 98-99 and 104 fail to teach using dipeptide as stabilizers and gamma irradiation. The Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with a gamma irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time was made to modify the method claims of the copending Application No. 09/942,941 by including the dipeptide carnosine as taught by the Hanna reference since carnosine is known to protect irradiated biological material (page 265, lines 1-4).

10. Claims 92, 125-128 and 116-119 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 107 and 109-114 of copending Application No. 09/942,941.

Claims 107 and 109-114 of copending Application No. 09/942,941 fully suggest claims 92, 125-128 and 116-119 of Application No. 09/925,619.

11. Claims 86-87 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-3, 5-6, 68 and 73 of US Patent No. 6,696,060.

Claims 5-6, 5-6, 68 and 73 of US Patent No. 6,696,060 fully suggest claims 86-87 of Application No. 09/925,619.

12. Claims 86-128 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 91-126 of U.S. Application No. 09/960,703.

Claims 91-126 of U.S. Application No. 09/960,703 fully suggest claims 86-128 of Application No. 09/925,619.

13. Claims 77 and 86 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 265-266 and 272-274 of copending Application No. 09/925,620 in view of Hanna et al (Free Rad. Res. Comms-IDS).

Claims 265-266 and 272-274 of Application No. 09/925,620 teaches a method for sterilizing biological material, which it can be a protein sample where a stabilizer is added and followed by an irradiation step. However, claims 265-266 and 272-274 fail to teach using dipeptide as stabilizers and gamma irradiation. The Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with a gamma irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time was made to modify the method claims of the copending Application No. 09/925,620 by including the

dipeptide carnosine as taught by the Hanna reference since carnosine is known to protect irradiated biological material (page 265, lines 1-4).

14. Claims 77, 86 and 97 of Application No. 09/925,619 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-4, 33, 47, 49, 53 and 85 of US Patent No. 6,682,695.

Claims 3-4, 33, 47, 49, 53 and 85 of US Patent No. 6,682,695 fully suggest claims 77, 86 and 97 of Application No. 09/925,619 (protein or serum or plasma is biological fluid).

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 77, 84-86, 88-91, 93-96, 100106 and 109-128 are rejected under 35 U.S.C. 102(e) as being anticipated by Grieb et al (US 2004/0249135).

17. The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

With respect to claims 77, 86 and 97, the Grieb reference teaches a method for sterilizing immunoglobulin solutions (paragraph 0021) that include adding a dipeptide stabilizer (paragraph 0023) and then gamma irradiating the solution (paragraph 0056).

With respect to claims 84-85, 88-91, 93-96, 100-106 and109-128, the Grieb reference teaches the following: tissue is maintained in an inert and vacuum atmosphere during irradiation (paragraph 0065), protein sample includes two different proteins (paragraph 0041), protein is a polyclonal immunoglobulin (paragraph 0041, IgG), immunoglobulin IgG (paragraph 0041), protein is albumin (paragraph 0086), concentration of dipeptide is at least 20mM (paragraph 0138) or at least 50 mM (paragraph 0078) or at least 100 mM (paragraph 0164), dipeptide is a homologous glycine-glycine (paragraph 0164), stabilizer not a dipeptide such as DMSO (paragraph 0053), two stabilizers that are not dipeptides such as DMSO and mannitol (paragraph 0053), contacting with a sensitizer (paragraph 0055), residual solvent such as water or ethanol that is produced by lyophilization (paragraphs 0054 and 0065), the residual solvent is less than 2.0% or less than 1.0% or less than 0.5% or less than 0.2% (paragraph 0061), irradiating for a sufficient time and amount to reduce the level of pathogens in the protein sample (paragraph 0056), rate of gamma radiation is at least 3.0 kGy/hr or at least 16 kGy/hr or at least 30 kGy/hr (paragraphs 0068-0069) and total dose of gamma radiation is 45 kGy (paragraph 0140).

18. Claims 77, 84-86, 88-91, 93-96, 100106 and 109-128 are rejected under 35 U.S.C. 102(e) as being anticipated by Grieb et al (U.S.P.N. 6,696,060).

19. The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

With respect to claims 77, 86 and 97, the Grieb reference teaches a method for sterilizing immunoglobulin solutions (col.4, lines 33-35) that include adding a dipeptide stabilizer (col.4, lines 58-59 and col.5, line 18) and then gamma irradiating the solution (col.13, lines7-8).

With respect to claims 84-85, 88-91, 93-96, 100-106 and109-128, the Grieb reference teaches the following: tissue is maintained in an inert and vacuum atmosphere during irradiation (col.14, lines 15-20), protein sample includes two different proteins (col.6, lines 30-32), protein is a polyclonal immunoglobulin (col.6, line 31, IgG), immunoglobulin IgG (col.6, line 31), protein is albumin (col.16, line 3), concentration of dipeptide is at least 20mM (col.21, line 59) or at least 50 mM (col.22, line 56) or at least 100 mM (col.22, line 56), dipeptide is a homologous glycine-glycine (col.21, line 59), stabilizer not a dipeptide such as DMSO (col.11, line 67), two stabilizers that are not dipeptides such as DMSO and mannitol (col.11, lines 50 and 67), contacting with a sensitizer (col.12, lines 38-40), residual solvent such as water or ethanol that is

produced by lyophilization (col.12, lines 15-20 and col.8, lines 30-32), the residual solvent is less than 2.0% or less than 1.0% or less than 0.5% or less than 0.2% (col.13, lines 63-67), irradiating for a sufficient time and amount to reduce the level of pathogens in the protein sample (col.13, lines 48-51), rate of gamma radiation is at least 3.0 kGy/hr or at least 16 kGy/hr or at least 30 kGy/hr (col.15, lines 3-8) and total dose of gamma radiation is 45 kGy (col.21, line 24).

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 78-83, 87 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claims 77, 86 and 97 and further in view of Fideler et al (Gamma Irradiation: Effects on Biomechanical Properties of Human Bone-Patellar Tendon-Bone Allografts-IDS).

The teachings of the Grieb reference have previously been set forth with respect to claims 77, 84-86, 88-91, 93-96, 100106 and 109-128; however, with respect to claims 78-83, 87 and 99, the Grieb reference fails to teach that the tissue is a hard or soft tissue or combination of hard and soft tissues and during gamma irradiation, the tissue is maintained below its freezing point. With respect to claims 78-83, 87 and 99, the Fideler reference teaches the following: the tissue is bone (page 643, right column, line 1), the tissue is a tendon (page 644, left column, line 3), the tissue is a combination of bone and tendon tissues (page 644, left column, line 22) and during gamma irradiation, and the tissue is maintained below its freezing point (page 644, left column, lines 33-37). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including pathogens inactivation of bone and soft tissues as taught by the Fideler reference since such tissues are of interest to orthopaedic surgeons for knee ligament reconstruction surgeries such as patellar tendon reconstruction surgery (page 643, right column, lines 1-9).

24. Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claim 91and further in view of Hackett (WO 91/16060).

With respect to claim 92, the Grieb reference fails to teach the use of clotting factors; however, the Hackett reference teaches the decontaminating protein fractions that contain clotting factors (page 2, line 22) such factor VIII (page 2, line 25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including clotting factors as taught by the Hackett reference since contamination problems still exist for blood plasma protein fractions that include clotting factors (page 2, lines 20-22).

25. Claim 98 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claim 97 and further in view of Platz et al (U.S.P.N. 5,418,130).

With respect to claim 98, the Grieb reference fails to teach that the serum is fetal bovine serum; however, the Platz reference teaches inactivating fetal bovine serum preparations (col.1, lines 24-25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by inactivating fetal bovine serum preparations as taught by the Platz reference since fetal bovine serum preparations are used as cell culture media (col.1, lines 24-26).

26. Claim 107 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to 97and further in view of Hanna et al (Free Rad. Res. Comms-IDS).

With respect to claim 107, the Grieb reference fails to teach the use of a heterologous dipeptide such as carnosine; however, the Hanna reference teaches that the heterologous dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including carnosine since it is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

27. Claim 108 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to 106 and further in view of Hanna et al (Free Rad. Res. Comms-IDS).

With respect to claim 108, the Grieb reference fails to teach the use of a heterologous dipeptide such as carnosine; however, the Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including carnosine since it is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

28. Claims 78-83, 87 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claims 77, 86 and 97

and further in view of Fideler et al (Gamma Irradiation: Effects on Biomechanical Properties of Human Bone-Patellar Tendon-Bone Allografts-IDS).

The teachings of the Grieb reference have previously been set forth with respect to claims 77, 84-86, 88-91, 93-96, 100106 and 109-128; however, with respect to claims 78-83, 87 and 99, the Grieb reference fails to teach that the tissue is a hard or soft tissue or combination of hard and soft tissues and during gamma irradiation, the tissue is maintained below its freezing point. With respect to claims 78-83, 87 and 99, the Fideler reference teaches the following: the tissue is bone (page 643, right column, line 1), the tissue is a tendon (page 644, left column, line 3), the tissue is a combination of bone and tendon tissues (page 644, left column, line 22) and during gamma irradiation, and the tissue is maintained below its freezing point (page 644, left column, lines 33-37). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including pathogens inactivation of bone and soft tissues as taught by the Fideler reference since such tissues are of interest to orthopaedic surgeons for knee ligament reconstruction surgeries such as patellar tendon reconstruction surgery (page 643, right column, lines 1-9).

29. Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claim 91and further in view of Hackett (WO 91/16060).

With respect to claim 92, the Grieb reference fails to teach the use of clotting factors; however, the Hackett reference teaches the decontaminating protein fractions

that contain clotting factors (page 2, line 22) such factor VIII (page 2, line 25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including clotting factors as taught by the Hackett reference since contamination problems still exist for blood plasma protein fractions that include clotting factors (page 2, lines 20-22).

30. Claim 98 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to claim 97 and further in view of Platz et al (U.S.P.N. 5,418,130).

With respect to claim 98, the Grieb reference fails to teach that the serum is fetal bovine serum; however, the Platz reference teaches inactivating fetal bovine serum preparations (col.1, lines 24-25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by inactivating fetal bovine serum preparations as taught by the Platz reference since fetal bovine serum preparations are used as cell culture media (col.1, lines 24-26).

31. Claim 107 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to 97and further in view of Hanna et al (Free Rad. Res. Comms-IDS).

With respect to claim 107, the Grieb reference fails to teach the use of a heterologous dipeptide such as carnosine; however, the Hanna reference teaches that the heterologous dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have

been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including carnosine since it is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

32. Claim 108 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grieb et al (US 2004/0249135) as applied to 106 and further in view of Hanna et al (Free Rad. Res. Comms-IDS).

With respect to claim 108, the Grieb reference fails to teach the use of a heterologous dipeptide such as carnosine; however, the Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Grieb reference by including carnosine since it is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

33. Claims 77, 86, 90-92, 95, 97, 107, 109, 114-117 and119-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS).

With respect to claims 77, 86 and 97, the Hackett reference discloses a method and a composition for inactivating biological fluids (page 3, lines 1-5 and examples on pages 22-26) where the level of active biological contaminants in a tissue (i.e., blood) or a protein sample (page 2, line 32) or plasma (page 6, lines 24) is reduced by adding an amino acid stabilizer (page 17, lines 5-7) to the material at an intrinsic amount to protect the material and then irradiating the biological material using gamma radiation (page 5,

lines 23-27). The Hackett reference teaches adding nucleic acids to biological material to be irradiated (page 7, lines 10-12) such that this teaching of adding amino acids is inclusive of adding polypeptides, dipeptides, or peptides; however, with respect to claims 77, 86 and 97, the Hackett reference fails to explicitly disclose adding a dipeptide. The Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by substituting one type of amino acid for another since carnosine is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

With respect to claims 90-92, 95, 109, 114-117 and 119-128, the Hackett reference teaches the following: sample contains at least two different proteins (page 2, lines 21-22), clotting factors (page 2, line 22), factor VIII (page 2, line 25) albumin (page 6, line 27), stabilizer that is not a dipeptide (page 3, lines 20-23 and page 4, line 2 where the stabilizer, for example, is monosaccharide), contacting the protein sample with one sensitizer (page 17, line 17 where the sensitizer is a polypeptide), the protein sample contains one residual solvent (page 4, lines 26-27), where is the residual solvent is water (page 4, line 27) or an organic solvent (page 7, lines 20-22 where the organic solvent is a carbohydrate), residual solvent is reduced by lyophilization, residual solvent is less than 2.0% or less than 1.0% or less than 0.5% or less than 0.2% (page 9, lines 21-22) and gamma irradiating the biological material for a sufficient time and energy to reduce (i.e., destroy viruses) contaminants in protein sample (page 5, lines

23-27). Regarding the gamma irradiation rates, the Hackett reference provides, for example, on page 15, lines 10-16, intensity and time ranges for irradiating the biological material. Upon unit conversion, the radiation rates were found to fall between 1.80 and 25 kGy/hour for a 6-log microorganism reduction. However, absence of evidence of advantage the disclosed gamma irradiation energy values, depending on the degree of inactivation intended and the sensitivity of biological materials modifying such a teaching to lower or higher doses is a matter of routine experimentation.

With respect to claim 107, the Hackett reference fails to teach adding a heterologous dipeptide stabilizer; however, the Hanna reference teaches adding carnosine, which is a heterologous dipeptide, to protect biological materials (preserve) in combination with a gamma irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by substituting one type of amino acid for another since carnosine is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

34. Claims 78-83, 87 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claims 77, 86 and 97 and further in view of Fideler et al (Gamma Irradiation: Effects on Biomechanical Properties of Human Bone-Patellar Tendon-Bone Allografts-IDS).

With respect to claims 78-83, 87 and 99, both the Hackett reference and the Hanna reference fail to teach that the tissue is a hard or soft tissue or combination of

hard and soft tissues and during gamma irradiation, the tissue is maintained below its freezing point. With respect to claims 78-83, 87 and 99, the Fideler reference teaches the following: the tissue is bone (page 643, right column, line 1), the tissue is a tendon (page 644, left column, line 3), the tissue is a combination of bone and tendon tissues (page 644, left column, line 22) and during gamma irradiation, and the tissue is maintained below its freezing point (page 644, left column, lines 33-37). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by including pathogens inactivation of bone and soft tissues as taught by the Fideler reference since such tissues are of interest to orthopaedic surgeons for knee ligament reconstruction surgeries such as patellar tendon reconstruction surgery (page 643, right column, lines 1-9).

35. Claims 84-85, 88-89 and 100-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claims 77, 86 and 97 and further in view of Lee et al (U.S.P.N. 5,485,496).

With respect to claims 84-85, 88-89 and 100-101, both the Hackett reference and the Hanna reference fail to teach that during irradiation, to maintain the tissue or the protein sample or the plasma in an inert atmosphere and under vacuum. With regard to claims 84-85, 88-89 and 100-101, the Lee reference, which is in the art sterilizing biomaterials such as absorbable vascular grafts tissues by applying gamma radiation, teaches that while gamma irradiating the biomaterial items, inert and vacuum conditions are maintained (col.1, lines 58-67 and col.2, lines 1-6). As a result, it would have been

obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by maintaining tissues under inert and vacuum conditions during irradiation as taught by the Lee reference since gamma irradiating in the absence of oxygen at very low temperatures provide improved strength properties (col.1, lines 51-57).

36. Claims 93-94, 96, 110-112 and 118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claims 91, 90, 97 and 115 and further in view of Wiesehahn et al (U.S.P.N. 4,727,027).

With respect to claims 93-94, 96, 110-112 and 118, both the Hackett reference and the Hanna reference fail to teach the following: immunoglobulin is a polyclonal, immunoglobulin is immunoglobulin IgA, protein produced by recombinant methods, stabilizer is ascorbic acid, two stabilizers that are not dipeptides, Stabilizer such as DMSO and the organic solvent is ethanol. With respect to claims 93-94, 96, 110-112 and 118, the Wiesehahn reference teaches the following: immunoglobulin is a polyclonal (col.2, line 47 where IgG is a polyclonal immunoglobulin), immunoglobulin is immunoglobulin IgA (col.2, line 47), protein produced by recombinant methods (col.2, line 52), stabilizer is ascorbic acid (col.5, line 3), two stabilizers that are not dipeptides (for example, glutathione and ascorbic acid as taught in col.5, line 3 and col.4, lines 47-48), Stabilizer such as DMSO (col.3, line 18) and the organic solvent is ethanol (col.3, line 18). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by adding DMSO as

taught by the Wiesehahn reference since DMSO addition result in shorter irradiation times (col.3, lines 18-28).

37. Claim 98 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claim 97 and further in view of Platz et al (U.S.P.N. 5,418,130).

With respect to claim 98, both the Hackett reference and the Hanna reference fail to teach that the serum is fetal bovine serum; however, the Platz reference teaches inactivating fetal bovine serum preparations (col.1, lines 24-25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by inactivating fetal bovine serum preparations as taught by the Platz reference since fetal bovine serum preparations are used as cell culture media (col.1, lines 24-26).

38. Claim 113 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) and Wiesehahn et al (U.S.P.N. 4,727,027) as applied to claim 112 and further in view of Platz et al (U.S.P.N. 5,418,130).

With respect to claim 113, the Hackett reference, the Hanna reference and the Wiesehahn reference all fail to teach that the serum is fetal bovine serum; however, the Platz reference teaches inactivating fetal bovine serum preparations (col.1, lines 24-25). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by inactivating fetal bovine

serum preparations as taught by the Platz reference since fetal bovine serum preparations are used as cell culture media (col.1, lines 24-26).

39. Claims 102-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claim 97 and further in view of Cook et al (U.S.P.N. 6,270,952).

With respect to claims 102-104, both the Hackett reference and the Hanna reference fail to teach dipeptide concentration ranges of 20 mM or 50 mM or 10mM; however, the Cook reference, which is in the art of inactivating biological fluids, teaches that a dipeptide such as GlyCys can be added to the biological fluid (col.13, lines 29-32) and also teaches that the concentration of the dipeptide can be in the range 0.1 mM to 30 mM (col.20, lines 63-65). In addition, the Cook reference does not limit the concentration of the dipeptide to the disclosed range and teaches that the concentration of the dipeptide and the pathogen-inactivating agent can be adjusted as needed (col.20, lines 57-62). However, absence of evidence of advantage of the recited dipeptide concentration values, depending on the degree of desired reduction of unwanted side reactions and while protecting the properties of the biological molecules and yet achieving the desired log kill of pathogens such recited concentration values of the dipeptide is a matter of routine experimentation.

40. Claims 105-106 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hackett (WO 91/16060) in view of Hanna et al (Free Rad. Res. Comms-IDS) as applied to claim 97 and further in view of Kessler et al (U.S.P.N. 5,648,075).

With respect to claims 105-106, both the Hackett reference and the Hanna reference fail to teach the use of a homologous dipeptide such glycine-glycine; however, the Kessler reference, which is in the art of inactivating pathogens in biological materials, teaches the use of glycine-glycine as a homologous dipeptide (col.7, lines 11-13). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by including glycine-glycine dipeptide as taught by the Kessler reference since it is a suitable buffering agent for biological solutions (col.7, lines 11-13).

With respect to claim 108, both the Hackett reference and the Kessler reference fail to teach the use of a heterologous dipeptide such as carnosine; however, the Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by including carnosine since it is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

Response to Arguments

41. Applicant's arguments with respect to claims 77-128 have been considered but are moot in view of the new ground(s) of rejection.

On page 10 of the Remarks section, applicant argues that, "Contrary to the Examiner's assertion, nothing in Hackett teaches or suggests the use of dipeptides as stabilizers." The examiner disagrees. Instant claims 77, 86 and 97 recites dipeptide

stabilizer only without providing a function. The Hackett reference teaches adding nucleic acids to biological material to be irradiated (page 7, lines 10-12) such that this teaching of adding amino acids is inclusive of adding polypeptides, dipeptides, or peptides. Amino acids recited by the Hackett reference in addition to their explicit functions are intrinsically functioning as stabilizers as well. However, the Hackett reference fails to explicitly disclose adding a dipeptide. The Hanna reference teaches that the dipeptide carnosine does protect biological materials (preserve) when added in combination with an irradiation step (page 265, lines 1-4). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the Hackett reference by substituting one type of amino acid for another since carnosine is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

On page 10 of the Remarks section, applicant argues that, "In contrast, Applicants' claimed methods of irradiation do not require the use of a sensitizer." The examiner disagrees since Instant claims 77, 86 and 97 include the preamble "comprising" such that the use of a sensitizer is within the scope of the present claims.

On page 10 of the Remarks section, applicant argues that, "Hanna is limited to a discussion of the free radical scavenging activity of carnosine." The examiner disagrees. The Hanna reference teaches that dipeptide carnosine acts as a stabilizer of biomolecules such as the HRP enzyme against radicals produced by the gamma radiation (page 267, first and fifth paragraphs). Thus, it would have been obvious to one having ordinary skill at the time the invention was made to modify the method of the

Hackett reference by substituting one type of amino acid for another since carnosine is known to protect irradiated biological material as evidenced by Hanna reference on page 265, lines 1-4.

Conclusion

42. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MONZER R. CHORBAJI whose telephone number is (571) 272-1271. The examiner can normally be reached on M-F 6:30-3:00.

43. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JOHN KIM can be reached on (571) 272-1142. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

44. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/31/2005

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